Complete Summary

GUIDELINE TITLE

(1) Prevention and treatment of tuberculosis among patients with infected human immunodeficiency virus: Principles of therapy and revised recommendations.
(2) Notice to readers: updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors.
(3) Updated guidelines for the use of rifamycins for the treatment of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors.

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention (CDC). Updated guidelines for the use of rifamycins for the treatment of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2004 Jan 20. 6 p. [30 references]

Centers for Disease Control and Prevention. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: Principles of therapy and revised recommendations. MMWR Recomm Rep 1998 Oct 30;47(RR-20):1-58. [162 references] PubMed

Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitor. MMWR Morb Mortal Wkly Rep 2000 Mar 10;49(9):185-9. [10 references] PubMed

GUIDELINE STATUS

These guidelines update previous Centers for Disease Control and Prevention (CDC) recommendations for treating and preventing active tuberculosis (TB) among adults and children coinfected with human immunodeficiency virus (HIV):

- CDC. Tuberculosis and human immunodeficiency virus infection: Recommendations of the Advisory Committee for the Elimination of Tuberculosis (ACET). MMWR Morbid Mortal Wkly Rep 1989;38:236-8, 243-50.
- American Thoracic Society/CDC. Treatment of tuberculosis and tuberculosis infection in adults and children. Am J Respir Crit Care Med 1994;149:1359-74.
- CDC. Clinical update: impact of HIV protease inhibitors on the treatment of HIV-infected tuberculosis patients with rifampin. MMWR Morbid Mortal Wkly Rep 1996;45:921-5.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- On August 11, 2003, the U.S. Food and Drug Administration, through its MedWatch program, distributed important safety information from the Centers for Disease Control and Prevention (CDC). The CDC notified healthcare professionals of revised recommendations against the use of rifampin plus pyrazinamide for treatment of latent tuberculosis infection, due to high rates of hospitalization and death from liver injury associated with the combined use of these drugs. For more information on this MedWatch alert, please see the U.S. Food and Drug Administration Center for Drug Evaluation and Research (CDER) Web site.
- On January 19, 2005, the U.S. Food and Drug Administration (FDA) issued a public health advisory about recent safety-related changes to the nevirapine (Viramune®) label and about appropriate use of HIV triple combination therapy containing nevirapine. The Indications and Usage section now recommends against starting nevirapine treatment in women with CD4+cell counts greater than 250 cells/mm3 unless benefits clearly outweigh risks. This recommendation is based on a higher observed risk of serious liver toxicity in patients with higher CD4 cell counts prior to initiation of therapy. See the FDA Web site for more information.
- On June 10, 2005, Bristol-Myers Squibb and FDA notified healthcare professionals of revisions to the WARNINGS, PRECAUTIONS/Pregnancy and Information for Patients, and PATIENT INFORMATION sections of the prescribing information for Sustiva (efavirenz), indicated in the treatment of HIV-1 infection. The revisions are a result of four retrospective reports of neural tube defects in infants born to women with first trimester exposure to Sustiva, including three cases of meningomyelocele and one Dandy Walker Syndrome. As Sustiva may cause fetal harm when administered during the first trimester to a pregnant woman, pregnancy should be avoided in women receiving Sustiva. An antiretroviral pregnancy registry has been established to monitor fetal outcomes of pregnant women exposed to Sustiva. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Tuberculosis (TB)
- Human immunodeficiency virus (HIV) infection

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Prevention
Treatment

CLINICAL SPECIALTY

Family Practice
Infectious Diseases
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To inform the reader of updated recommendations and guidelines for the diagnosis, treatment, and prevention of tuberculosis (TB) among patients with human immunodeficiency virus (HIV) in the United States
- To guide clinical practice and policy development related to appropriate management of patients with or at risk for HIV-related TB.

TARGET POPULATION

Human immunodeficiency virus (HIV)-infected adults and children with active or latent tuberculosis or at risk of getting tuberculosis

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Medical history
2. Chest x-ray examination
3. Laboratory tests, including smears of sputum for acid-fast bacilli, sputum cultures, and drug susceptibilities; complete blood cell count, including platelets; chemistry panel tests, especially liver function tests
4. Other procedures, such as a baseline visual acuity exam and test for red-green color perception; baseline audiometry tests; bronchoscopies and bronchoalveolar lavage; biopsies and aspirates; mycobacterial culturing of nonrespiratory clinical specimens; and radiologic evaluations other than chest x-rays (e.g., computerized tomographies, magnetic resonance imaging)
5. Human immunodeficiency virus (HIV) counseling and testing.

Treatment

1. Direct observation therapy (DOT) and direct observation preventive therapy (DOPT) as strategies to promote adherence to therapy.
2. Coadministration of antituberculosis (rifamycins [rifampin, rifabutin, and rifapentine*] or non-rifamycins [isoniazid, streptomycin, pyrazinamide, and ethambutol]) and antiretroviral therapies (protease inhibitors [saquinavir, indinavir, ritonavir, lopinavir/ritonavir, atazanavir, saquinavir/ritonavir, fosamprenavir, and nelfinavir], nonnucleoside reverse transcriptase inhibitors [NNRTI] [nevirapine, delavirdine, and efavirenz], and nucleoside reverse transcriptase inhibitors [NRTI] [zidovudine, didanosine, zalcitabine, stavudine, and lamivudine]).

   *Rifapentine is considered but not recommended

3. Vitamin B6 (pyridoxine) supplementation
4. Administration of preventive therapy in HIV-infected patients with latent M. tuberculosis infection, including isoniazid, rifabutin and pyrazinamide, or rifampin and pyrazinamide.

Management

1. Monitoring for response to antituberculosis therapy, drug-related toxicity, and drug interactions by strategies such as monthly medical evaluations.
2. Diagnosis and management (symptomatic therapy and no change in antituberculosis or antiretroviral therapy or hospitalization and corticosteroid therapy) of paradoxical reactions.

MAJOR OUTCOMES CONSIDERED

- Tuberculosis (TB) relapse rates (recurrence of TB following successful completion of treatment)
- Early clinical response to therapy
- Conversion of M. tuberculosis sputum cultures from positive to negative

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence Supporting the Recommendation

I. At least one randomized trial with clinical endpoints
II. Clinical trials with laboratory endpoints only or conducted only in populations not infected with human immunodeficiency virus
III. Expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of the Recommendation

A. Strong; should always be offered
B. Moderate; should usually be offered
C. Optional
D. Should generally not be offered
E. Should never be offered

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The strength of the recommendation grades (A-E) and the quality of the evidence supporting the recommendation grades (I-III) are defined at the end of the "Major Recommendations" field.

Note from the National Guideline Clearinghouse: Previously updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis (TB) among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors are included in these recommendations (MMWR Morbid Mortal Wkly Rep 2000 Mar 10;49(09):185-9). The most current update (January 20, 2004) presents data pertaining to interactions between these agents with recommendations for their use, including initial recommendations for the protease inhibitors lopinavir/ritonavir, atazanavir, and fosamprenavir (a phosphate ester prodrug of amprenavir). The new information is also included in these recommendations.

Active Tuberculosis (TB)

Diagnosis of Human Immunodeficiency Virus (HIV)-Related Tuberculosis

Medical Evaluation of Patients Suspected of Having Active TB

Recommendation – A.II
Every person suspected of having TB should undergo a thorough medical evaluation.

Recommendation – A.II
The evaluation should include HIV counseling and testing unless the person has documentation of a) a positive HIV antibody test or b) a negative result to an HIV antibody test conducted within the past 6 months.

Management of HIV-Infected Patients with Active TB

Treatment Options for Patients with HIV Infection and Drug-Susceptible Pulmonary TB (Note: The Appendix in the original guideline document contains a table of recommended treatment options)

Recommendation – A.II
Direct observation therapy (DOT) and other strategies that promote adherence to therapy should be used for all patients with HIV-related TB.

Recommendation – A.II
For patients who are receiving therapy with protease inhibitors or nonnucleoside reverse transcriptase inhibitors (NNRTI), the initial phase of a 6-month TB regimen consists of isoniazid, rifabutin, pyrazinamide, and ethambutol. These drugs are administered a) daily for 8 weeks or b) daily for at least the first 2 weeks, followed by twice-a-week dosing for 6 weeks, to complete the 2-month induction phase. The second phase of treatment consists of isoniazid and rifabutin administered daily or twice a week for 4 months.

Recommendation – B.II
For patients for whom the use of rifamycins is limited or contraindicated for any reason (e.g., intolerance to rifamycins, patient/clinician decision not to combine antiretroviral therapy with rifabutin), the initial phase of a 9-month TB regimen consists of isoniazid, streptomycin, pyrazinamide, and ethambutol administered a) daily for 8 weeks or b) daily for at least the first 2 weeks, followed by twice-a-week dosing for 6 weeks, to complete the 2-month induction phase. The second phase of treatment consists of isoniazid, streptomycin,* and pyrazinamide administered 2-3 times a week for 7 months.

*Every effort should be made to continue administering streptomycin for the total duration of treatment or for at least 4 months after culture conversion (approximately 6-7 months from the start of treatment). Some experts suggest that in situations in which streptomycin is not included in the regimen for all of the recommended 9 months, ethambutol should be added to the regimen to replace streptomycin, and the duration of treatment should be prolonged from 9 months to 12 months. Alternatives to streptomycin are the injectable drugs amikacin, kanamycin, and capreomycin.

Recommendation – A.I
For patients who are not candidates for antiretroviral therapy, or for those patients for whom a decision is made not to combine the initiation of antiretroviral therapy with TB therapy, the preferred option continues to be a 6-month regimen that consists of isoniazid, rifampin, pyrazinamide, and ethambutol (or streptomycin). These drugs are administered a) daily for 8 weeks or b) daily for at least the first 2 weeks, followed by 2-3-times-per-week dosing for 6 weeks, to complete the 2-month induction phase. The second phase of treatment consists of a) isoniazid and rifampin administered daily or 2-3 times a week for 4 months. Isoniazid, rifampin, pyrazinamide, and ethambutol (or streptomycin) also can be administered three times a week for 6 months.

Recommendation – D.II
TB regimens consisting of isoniazid, ethambutol, and pyrazinamide (i.e., three-drug regimens that do not contain a rifamycin, an aminoglycoside [e.g., streptomycin, amikacin, kanamycin], or capreomycin) should generally not be used for the treatment of patients with HIV-related TB; if these regimens are used for the treatment of TB, the minimum duration of therapy should be 18 months (or 12 months after documented culture conversion).

Recommendation – A.II
Pyridoxine (vitamin B6) (25-50 mg daily or 50-100 mg twice weekly) should be administered to all HIV-infected patients who are undergoing TB treatment with isoniazid, to reduce the occurrence of isoniazid-induced side effects in the central and peripheral nervous system.

Recommendation – E.II
Because CDC's most recent recommendations for the use of antiretroviral therapy strongly advise against interruptions of therapy,* and because alternative TB treatments that do not contain rifampin are available, previous antituberculosis therapy options that involved stopping protease inhibitor therapy to allow the use of rifampin (Option I and Option II [CDC, 1996]) are no longer recommended.

*To minimize the emergence of drug-resistant HIV strains, if any antiretroviral medication must be temporarily discontinued for any reason, clinicians and patients should be aware of the theoretical advantage of stopping all antiretroviral agents simultaneously, rather than continuing the administration of one or two of these agents alone ("Report of the NIH Panel," 1998).

Medications and Doses for Treatment of TB (Note: The Appendix of the original guideline document contains a table on the doses, toxicities, and monitoring requirements of antituberculosis medications.)

Recommendation – No rating
When rifabutin is used concurrently with indinavir, nelfinavir, or amprenavir, the recommended daily dose of rifabutin should be decreased from 300 mg to 150 mg.

Recommendation – No rating
The dose of rifabutin recommended for twice-weekly administration is 300 mg, and this dose recommendation does not change if rifabutin is used concurrently with indinavir, nelfinavir, or amprenavir.

Recommendation – No rating
Preliminary drug interaction studies suggest that when rifabutin is used concurrently with efavirenz, the dose of rifabutin for both daily and twice-weekly administration should be increased from 300 mg to 450 mg. See special notices below.

Recommendation – No rating
Three-times-per-week administration of rifabutin used in combination with antiretroviral therapy has not been studied, and thus a recommendation for adjustment of dosages cannot currently be made.

Recommendation – B.II
Experts do not know whether the daily dose of rifabutin should be reduced when this drug is used concurrently with either soft-gel saquinavir (Fortovase™) or nevirapine.

Recommendation – No rating
No modifications in the usually recommended doses of isoniazid, ethambutol,

pyrazinamide, or streptomycin are necessary if these drugs are used concurrently with protease inhibitors, NNRTIs, or nucleoside reverse transcriptase inhibitors (NRTIs).

Recommendation – No rating
The safety and effectiveness of rifapentine (Priftin®), a rifamycin newly approved by the U.S. Food and Drug Administration for the treatment of pulmonary tuberculosis, have not been established for patients infected with HIV. Administration of rifapentine to patients with HIV-related TB is not currently recommended.

Duration of TB Treatment

Recommendation – A.II
The minimum duration of short-course rifabutin-containing TB treatment regimens is 6 months, to complete a) at least 180 doses (one dose per day for 6 months) or b) 14 induction doses (one dose per day for 2 weeks) followed by 12 induction doses (two doses per week for 6 weeks) plus 36 continuation doses (two doses per week for 18 weeks).

Recommendation – A.II
The minimum duration of short-course rifampin-containing TB treatment regimens is 6 months, to complete a) at least 180 doses (one dose per day for 6 months) or b) 14 induction doses (one dose per day for 2 weeks) followed by 12-18 induction doses (two to three doses per week for 6 weeks) plus 36-54 continuation doses (two to three doses per week for 18 weeks).

Recommendation – A.II
Three-times-per-week rifampin regimens should consist of at least 78 doses administered over 26 weeks.*

*Three-times-per-week rifabutin regimens, used in combination with antiretroviral therapy, have not been studied.

Recommendation – A.II
The final decision on the duration of therapy should consider the patient's response to treatment. For patients with delayed response to treatment, the duration of rifamycin-based regimens should be prolonged from 6 months to 9 months (or to 4 months after culture conversion is documented).

Recommendation – A.II
The minimum duration of non-rifamycin, streptomycin-based TB treatment regimens is 9 months, to complete a) at least 60 induction doses (one dose per day for 2 months) or b) 14 induction doses (one dose per day for 2 weeks) followed by 12-18 induction doses (two to three doses per week for 6 weeks) plus either 60 continuation doses (two doses per week for 30 weeks) or 90 continuation doses (three doses per week for 30 weeks).

Recommendation – A.II
When making the final decision on the duration of therapy, clinicians should consider the patient's response to treatment. For patients with delayed response

to treatment, the duration of streptomycin-based regimens should be prolonged from 9 months to 12 months (or to 6 months after culture conversion is documented).

Recommendation – A.III
Interruptions in therapy because of drug toxicity or other reasons should be taken into consideration when calculating the end-of-therapy date for individual patients. Completion of therapy is based on total number of medication doses administered and not on duration of therapy alone.

Recommendation – A.III
Reinstitution of therapy for patients with interrupted TB therapy might require a continuation of the regimen originally prescribed (as long as needed to complete the recommended duration of the particular regimen) or a complete renewal of the regimen. In either situation, when therapy is resumed after an interruption of greater than or equal to 2 months, sputum samples (or other clinical samples as appropriate) should be taken for smear, culture, and drug-susceptibility testing.

Management of the Co-administration of TB and HIV Therapies, Including the Potential for Paradoxical Reactions

Monthly Medical Evaluation and the Diagnosis and Management of Paradoxical Reactions

Recommendation – A.II
All patients should receive a monthly clinical evaluation to monitor their response to treatment, adherence to treatment, and medication side effects. During the early days of therapy, the interval between these evaluations might be shorter (e.g., every 2 weeks).

Recommendation – A.II
Patients suspected of having paradoxical reactions should be evaluated to rule out other causes for their clinical presentation (e.g., TB treatment failure) before attributing their signs and symptoms to a paradoxical reaction.

Recommendation – C.III
Some experts recommend that to avoid paradoxical reactions, clinicians should delay the initiation of or changes in antiretroviral therapy until the signs and symptoms of TB are well controlled (possibly 4-8 weeks from the initiation of TB therapy).

Recommendation – No rating
For patients with a paradoxical reaction in whom the symptoms are not severe or life-threatening, the management of these reactions might consist of symptomatic therapy and no change in antituberculosis or antiretroviral therapy. For patients with a paradoxical reaction associated with severe or life-threatening clinical manifestations (e.g., uncontrollable fever, airway compromise from enlarging lymph nodes, enlarging serosal fluid collections [pleuritis, pericarditis, peritonitis], sepsis-like syndrome), the management might include hospitalization and possibly a time-limited use of corticosteroids (e.g., prednisone started daily at a dose of 60-80 mg and reduced after 1 or 2 weeks, with the resolution of symptoms as a guide; in most cases, corticosteroid therapy should last no more than 4-6 weeks).

TB Drug Interaction and Absorption

Recommendation – E.II
Given the expected drug interactions that would result in markedly decreased serum levels of antiretroviral agents, and given the overlapping toxicities, the coadministration of rifampin with any of the protease inhibitors or with NNRTIs, as well as the coadministration of rifabutin with ritonavir, hard-gel saquinavir (Invirase™), or delavirdine, is contraindicated. See special notices below.

Recommendation - A.II
The potent effect of rifampin as a CYP450 inducer, which lowers the serum concentration of protease inhibitors and NNRTIs, is expected to continue up to at least 2 weeks following the discontinuation of rifampin. Therefore, to diminish the likelihood of adverse effects on drug metabolism, clinicians should plan the start of therapy with protease inhibitors or NNRTIs at least 2 weeks after the date of the last dose of rifampin.

Recommendation - A.II
Rifabutin is a less potent CYP450 inducer than rifampin and thus can be used (with adjustments in dosages) concurrently with the NNRTIs nevirapine or efavirenz or with certain protease inhibitors (e.g., indinavir, nelfinavir, and possibly soft-gel saquinavir [Fortovase™] and amprenavir).

Recommendation - No rating
Indinavir serum concentrations are decreased by rifabutin-related induction of the hepatic cytochrome P450; therefore, when indinavir is used in combination with rifabutin, the dose of indinavir usually is increased from 800 mg every 8 hours to 1,200 mg every 8 hours.

Recommendation - No Rating
Nelfinavir serum concentrations are also decreased when nelfinavir is used in combination with rifabutin; however, the resultant metabolite of nelfinavir is known to be active against HIV. Nevertheless, some experts suggest increasing the dose of nelfinavir from 750 mg three times per day to 1,000 mg three times per day when used in combination with rifabutin.

Recommendation - No Rating
Experts do not know whether dose-modifications are needed for soft-gel saquinavir (Fortovase™), amprenavir, nevirapine, or efavirenz if these agents are used in combination with rifabutin.

Recommendation - No Rating
Many other medications commonly used by patients with HIV infection have drug interactions with the rifamycins (rifampin or rifabutin) of sufficient magnitude to require interventions such as dose adjustments or use of alternative therapies. Some examples of these drugs are hormonal contraceptives, dapsone, ketoconazole, fluconazole, itraconazole, narcotics (including methadone), anticoagulants, corticosteroids, cardiac glycosides, hypoglycemics (sulfonylureas), diazepam, beta-blockers, anticonvulsants, and theophylline.

Recommendation - No Rating
Malabsorption of antituberculosis drugs has been demonstrated in some patients

with HIV infection, and in some cases, it has been associated with TB treatment failures and the selection of drug-resistant M. tuberculosis bacilli (Sahai et al., 1997; Peloquin et al., 1996; Berning et al., 1992; Patel, Belmonte, & Crow, 1995; Peloquin, MacPhee, & Berning, 1993). Therapeutic drug monitoring has been advocated by some experts as an adjunct in the management of HIV-related TB (Peloquin, 1997). This approach might be useful when evaluating patients with TB treatment failure or relapse and in the treatment of multidrug-resistant (MDR) TB. However, the role of therapeutic drug monitoring in the routine management of TB among HIV-infected patients has not been established and is not presently recommended.

Special Notice: On March 10, 2000 the CDC issued a notice of updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of TB among HIV-infected patients taking protease inhibitors or NNRTIs (MMWR Morb Mortal Wkly Rep. 2000, Mar 10/49(09); 185-9).

The use of rifampin to treat active TB was specifically contraindicated for patients who take any of the protease inhibitors or NNRTIs, and the use of rifabutin was contraindicated for patients taking the protease inhibitor ritonavir or the NNRTI delavirdine. New data indicate that rifampin can be used for the treatment of active TB in three situations:

- In a patient whose antiretroviral regimen includes the NNRTI efavirenz (Benedek, Joshi, & Fiske, 1998) and two NRTIs
- In a patient whose antiretroviral regimen includes the protease inhibitor ritonavir (Abbott Laboratories, 1999) and one or more NRTIs
- In a patient whose antiretroviral regimen includes the combination of two protease inhibitors (Veldkamp et al., 1999) (ritonavir and either saquinavir hard-gel capsule (HGC) or saquinavir soft-gel capsule (SGC)

In addition, the updated guidelines recommend substantially reducing the dosage of rifabutin (150 mg two or three times per week) when it is administered to patients taking ritonavir (Gallicano et al., 2000) (with or without saquinavir HGC or saquinavir SGC) and increasing the dose of rifabutin (either 450 mg or 600 mg daily or 600 mg two or three times per week) when rifabutin is used concurrently with efavirenz (Benedek et al., 1998).

For patients treated with two protease inhibitors, the complexity of drug interactions is amplified and recommendations about dose modifications are difficult when rifamycins also are administered. However, if ritonavir (taken in doses ranging from 100 mg to 600 mg twice per day) is combined with any other protease inhibitors for HIV therapy, and the administration of rifabutin also becomes necessary, the need to use substantially reduced doses of rifabutin (150 mg two or three times per week) is certain. In comparison, for a patient who is undergoing treatment with saquinavir SGC (a relatively weak CYP450 inhibitor) (CDC, 1998) and two NRTIs, the usual dosage (300 mg daily or two or three times per week) of rifabutin should not be decreased (Jorga, 1999). When both an inhibitor and an inducer of CYP450 are used with rifamycins (e.g., a protease inhibitor in combination a NNRTI), a different complex interaction occurs and the appropriate drug-dose adjustments necessary to ensure optimum levels of both antiretroviral drugs and rifamycins are unknown.

See Table 1 in the updated original guideline document for recommendations for coadministering different antiretroviral drugs with the antimycobacterial drugs rifabutin and rifampin (Notice to Readers: Updated Guidelines for the Use of Rifabutin or Rifampin for the Treatment and Prevention of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors. MMWR Morb Mortal Wkly Rep. 2000, Mar 10/49(09); 185-9).

Special Notice: On January 20, 2004 the CDC issued a notice of updated guidelines for the use of rifamycins for the treatment of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors.

Rifampin and Antiretroviral Therapy (refer to Table 1 in the updated original guideline document for recommendations for coadministering protease inhibitors and non-nucleoside reverse transcriptase inhibitors with rifampin)

Initial guidance from CDC stated that use of rifampin was contraindicated for persons taking NNRTIs and protease inhibitors. Subsequent data, however, have supported the use of rifampin with certain combinations of antiretroviral agents. These include:

- ritonavir with nucleoside/tide reverse transcriptase inhibitors (NRTIs)
- efavirenz with NRTIs

Alternative, less supported, antiretroviral combinations for use with rifampin include:

- ritonavir (400 mg twice daily) and saquinavir (400 mg twice daily) with NRTIs
- ritonavir (400 mg twice daily) and lopinavir (400 mg twice daily) with NRTIs (when the current coformulated lopinavir/ritonavir combination is supplemented with additional ritonavir, see Table 1 in the updated original guideline document)
- nevirapine with NRTIs
- triple NRTIs

Rifabutin and Antiretroviral Therapy (refer to Table 2 in the updated original guideline document for recommendations for coadministering protease inhibitors and non-nucleoside reverse transcriptase inhibitors with rifabutin)

Rifabutin could be used with most protease inhibitors, including atazanavir and fosamprenavir, provided the dose of rifabutin is reduced. Use of rifabutin with saquinavir alone is not advised given the significant decrease in saquinavir concentration; however, rifabutin may be used with saquinavir if coadministered with ritonavir. Other protease inhibitor/ritonavir combinations, including lopinavir/ritonavir, can be safely coadministered with rifabutin as long as the dose of rifabutin is decreased. Conversely, as a CYP3A4 inducer, efavirenz can reduce concentrations of rifabutin, necessitating an increase in the dose of rifabutin.

Other Drug-interaction Issues

Refer to the 2003 updated original guideline document for a discussion of other drug-interaction issues.

Treatment of TB in Special Situations

The following general treatment recommendations address special situations. Detailed recommendations for managing these patients are published elsewhere (Bass et al., 1994; Bureau of Tuberculosis Control, New York City Department of Health, 1997; Des Prez & Hass, 1995; Jeena et al., 1996; Davidson, 1995; Shafer et al., 1991) and consultation with experts in these areas is highly recommended.

Treatment of Drug-Resistant TB

Recommendation - A.II
TB disease resistant to isoniazid only. The treatment regimen should generally consist of a rifamycin (rifampin or rifabutin), pyrazinamide, and ethambutol for the duration of treatment. Intermittent therapy administered twice weekly can be used following at least 2 weeks (14 doses) of daily induction therapy (see Duration of TB Treatment). The recommended duration of treatment is 6 to 9 months or 4 months after culture conversion. Isoniazid is generally stopped when resistance (greater than 1% of bacilli resistant to 1.0 micrograms/mL of isoniazid) to this drug is discovered; however, when low-level resistance is discovered (greater than 1% of bacilli resistant to 0.2 micrograms/mL of isoniazid, but no resistance to 1.0 microg/mL of isoniazid), some experts suggest continuing to use isoniazid as part of the treatment regimen. Because the development of acquired rifamycin resistance would result in multidrug-resistant (MDR) TB, clinicians should carefully supervise and manage TB treatment for these patients.

Recommendation - A.II
TB disease resistant to rifampin only. The 9-month treatment regimen should generally consist of an initial 2-month phase of isoniazid, streptomycin, pyrazinamide, and ethambutol. The second phase of treatment should consist of isoniazid, streptomycin, and pyrazinamide administered for 7 months. Because the development of acquired isoniazid resistance would result in MDR TB, clinicians should carefully supervise and manage TB treatment for these patients.

2004 Update

Acquired Rifamycin Resistance

Rifamycin resistance has developed during the treatment of TB in HIV-infected persons, and has been associated with all rifamycins, particularly with highly-intermittent administration (once- or twice-weekly). Rifapentine, which can be administered once per week, is not recommended for HIV-infected patients because of their risk of developing rifamycin resistance. In addition, rifamycin resistance has developed in patients who have advanced HIV disease (i.e., CD4 < 100 cells/microliter) and are receiving rifampin or rifabutin twice weekly. To prevent acquired rifamycin resistance in persons with advanced HIV infection and TB, more frequent therapy (thrice-weekly or daily) with either rifampin or rifabutin-based TB regimens is recommended.

Recommendation - A.III
Multidrug-resistant TB (resistant to both isoniazid and rifampin). These patients should be managed by or in consultation with physicians experienced in the management of MDR TB. Findings from a retrospective study of patients with MDR TB strongly indicate that early aggressive treatment with appropriate regimens (based on the known or suspected drug-resistance pattern of the M. tuberculosis isolate) markedly decreases deaths associated with MDR TB (Schluger, 1999; Salomon et al., 1995; Park et al., 1996; Turett et al., 1995). Most drug regimens currently used to treat MDR TB include an aminoglycoside (e.g., streptomycin, kanamycin, amikacin) or capreomycin, and a fluoroquinolone. The recommended duration of treatment for MDR TB in HIV-seropositive patients is 24 months after culture conversion, and posttreatment follow-up visits to monitor for TB relapse should be conducted every 4 months for 24 months. Because of the serious personal and public health concerns associated with MDR TB, health departments should always use DOT for these patients and take whatever steps are needed to ensure their adherence to therapy.

TB Treatment for HIV-Infected Pregnant Women

Recommendation - A.III
HIV-infected pregnant women who have a positive M. tuberculosis culture or who are suspected of having TB disease should be treated without delay. Choices of TB treatment regimens for HIV-infected pregnant women are those that include a rifamycin. Routine use of pyrazinamide during pregnancy is recommended by international organizations but has not been recommended in the United States because of inadequate teratogenicity data (Bass et al., 1994). However, for HIV-infected pregnant women, the benefits of a TB treatment regimen that includes pyrazinamide outweigh potential pyrazinamide-related risks to the fetus. Aminoglycosides (e.g., streptomycin, kanamycin, amikacin) and capreomycin are contraindicated for all pregnant women because of potential adverse effects on the fetus. Considerations for antiretroviral therapy for pregnant HIV-infected women have been published elsewhere ("Report of the NIH Panel," 1998).

TB Treatment for HIV-Infected Children

Recommendation - A.II
HIV-infected children who are suspected of having TB disease should be treated without delay. For HIV-infected children, even those who are too young to be evaluated for visual acuity and red-green perception, ethambutol at a dosage of 15 mg/kg body weight should generally be included as part of the initial regimen, unless the infecting strain of M. tuberculosis is known or suspected of being susceptible to isoniazid and rifampin. If drug-susceptibility results are not available, a four-drug regimen (e.g., isoniazid, rifamycin, pyrazinamide, and ethambutol) for 2 months, followed by intermittent administration of isoniazid and a rifamycin for 4 months, is recommended. Considerations for antiretroviral therapy for children and adolescents have been published elsewhere ("Guidelines," 1998).

TB Treatment for HIV-Infected Patients with Extrapulmonary TB

Recommendation - A.II
The basic principles that support the treatment of pulmonary TB in HIV-infected

patients also apply to extrapulmonary forms of the disease. Most extrapulmonary forms of TB (including TB meningitis, tuberculous lymphadenitis, pericardial TB, pleural TB, and disseminated or miliary TB) are more common among persons with advanced-stage HIV disease (DeCock et al., 1992; Alpert et al., 1997) than among patients with asymptomatic HIV infection. The drug regimens and treatment durations that are recommended for treating pulmonary TB in HIV-infected adults and children are also recommended for treating most patients with extrapulmonary disease. However, for certain forms of extrapulmonary disease, such as meningioma, bone, and joint TB, using a rifamycin-based regimen for at least 9 months is generally recommended.

Latent M. tuberculosis Infection

Diagnosis of M. tuberculosis Infection Among HIV-Infected Persons

Tuberculin Skin Testing (TST) Among HIV-Infected Persons

Recommendation - A.I
As soon as possible after HIV infection is diagnosed, all persons should receive a TST unless previously tested and found to be TST-positive.

Recommendation - A.II
As soon as possible (ideally within 7 days) after learning of an exposure to a patient with infectious TB, all HIV-infected persons should be evaluated for TB and receive a TST, regardless of any previous TST results.

Recommendation - B.III
TSTs should be conducted periodically for HIV-infected persons who are TST-negative on initial evaluation and who belong to populations with a substantial risk of exposure to M. tuberculosis (e.g., residents of prisons, jails, or homeless shelters).

Recommendation - C.III
Some experts recommend repeat TSTs for HIV-infected persons because of effective antiretroviral therapy.

Recommendation - C.I
Because results of anergy testing in HIV-infected populations in the United States do not seem useful to clinicians making decisions about preventive therapy, anergy testing is no longer recommended as a routine component of TB screening among HIV-infected persons (CDC, 1997). However, some experts support the use of anergy testing to help guide individual decisions regarding preventive therapy, and some recommend that a TST be performed on patients previously classified as anergic if evidence indicates that these patients' immune systems have responded to therapy with antiretroviral drugs.

Candidates for TB Preventive Therapy Among HIV-Infected Persons

Recommendation - A.I
Persons with a TST reaction size of greater than or equal to 5 mm who have not

previously received treatment for M. tuberculosis infection should receive TB preventive treatment, regardless of their age.

Recommendation - A.II
Persons who have had recent contact with an infectious TB patient should receive TB preventive treatment, regardless of preventive treatment.

Recommendation - A.II
Persons with a history of prior untreated or inadequately treated past TB that healed and no history of adequate treatment for TB should receive TB preventive treatment, regardless of their age or results of TSTs.

Recommendation - C.III
Primary prophylaxis for TST-negative, HIV-infected persons with an on-going and unavoidable high risk of exposure to M. tuberculosis for the duration of the exposure time (e.g., residents of prisons, jails, or homeless shelters in which the current prevalence of TB is high) should be considered in some situations.

TB Preventive Therapy Regimens, Including Dosage Recommendations

The following recommendations are appropriate for adults with HIV infection who are likely to have latent M. tuberculosis infection with organisms susceptible to isoniazid and rifamycins. Updated recommendations for children are not yet available.

Recommended Preventive Therapy Regimens for Patients Receiving Protease Inhibitors or NNRTIs

Recommendation - A.II
For HIV-infected adults, a 9-month regimen of isoniazid can be administered daily.

Recommendation - B.I
For HIV-infected adults, a 9-month regimen of isoniazid can be administered twice a week (direct observation preventive therapy [DOPT] should be used with intermittent dosing regimens).

Recommendation - B.III
For HIV-infected adults, a 2-month regimen of rifabutin and pyrazinamide can be administered daily.

Recommendation - No rating
The concurrent administration of rifabutin is contraindicated with ritonavir, hard-gel saquinavir (Invirase™), and delavirdine.

Recommended Preventive Therapy Regimens for Patients Not Receiving Protease Inhibitors or NNRTIs

Recommendation - A.II
For HIV-infected adults, a 9-month regimen of isoniazid can be administered daily.

Recommendation - B.I
For HIV-infected adults, a 9-month regimen of isoniazid can be administered twice a week.

Recommendation - A.I
For HIV-infected adults, a 2-month regimen of rifampin and pyrazinamide can be administered daily.

Duration of TB Preventive Therapy

Recommendation - A.II
Daily isoniazid regimens should consist of at least 270 doses to be administered for 9 months or up to 12 months if interruptions in therapy occur.

Recommendation - A.III
Twice-a-week isoniazid regimens should consist of at least 76 doses to be administered for 9 months or up to 12 months if interruptions in therapy occur.

Recommendation - A.II
Daily regimens of rifamycin (rifampin or rifabutin) and pyrazinamide should consist of at least 60 doses to be administered for 2 months or up to 3 months if interruptions.

Recommendation - A.III
When calculating the end-of-preventive-therapy date for individual patients, consider interruptions in therapy because of drug toxicity or other reasons. Completion of therapy is based on total number of medication doses administered and not on duration of therapy alone.

Recommendation - A.III
When reinstituting therapy for patients with interrupted TB preventive therapy, clinicians might need to continue the regimen originally prescribed (as long as needed to complete the recommended duration of the particular regimen) or completely renew the entire regimen. In either situation, when therapy is restored after an interruption of greater than or equal to 2 months, a medical examination to rule out TB disease is indicated.

Monthly Monitoring of Patients During TB Preventive Treatment

Recommendation - A.II
All persons undergoing preventive treatment for TB should receive a monthly clinical evaluation of their adherence to treatment and medication side effects.

Treatment of Latent M. tuberculosis Infection in Special Situations

Recommendation - A.I
DOPT should always be used with intermittent dosing regimens.

Recommendation - B.III
DOPT also should be used when operationally feasible, especially with 2-month preventive therapy regimens and in some special settings (e.g., in some

institutional settings, in some community outreach programs, and for some persons who are candidates for preventive therapy because they are household contacts of patients with TB disease who are receiving home-based DOT).

Recommendation - A.III
For persons who are known to be contacts of patients with isoniazid-resistant, rifamycin-susceptible TB, a 2-month preventive therapy regimen of a rifamycin (rifampin or rifabutin) and pyrazinamide is recommended. For patients with intolerance to pyrazinamide, a 4-6-month regimen of a rifamycin (rifampin or rifabutin) alone is recommended ("A double-blind placebo-controlled clinical trial," 1992; Polesky et al., 1996; Villarino et al., 1997).

Recommendation - C.III
The choices for preventive treatment for persons who are likely to be infected with a strain of M. tuberculosis resistant to both isoniazid and rifamycins are published elsewhere ("Management of persons," 1992). In general, the recommended preventive therapy regimens for these persons include the use of a combination of at least two antituberculosis drugs that the infecting strain is believed to be susceptible to (e.g., ethambutol and pyrazinamide, levofloxacin and ethambutol). The clinician should review the drug-susceptibility pattern of the M. tuberculosis strain isolated from the infecting source-patient before choosing a preventive therapy regimen.

Recommendation - A.III
For HIV-infected women who are candidates for TB preventive therapy, the initiation or discontinuation of preventive therapy should not be delayed on the basis of pregnancy alone, even during the first trimester. A 9-month regimen of isoniazid administered daily or twice a week is the only recommended option.

Recommendation - No rating
For HIV-infected children who are candidates for TB preventive therapy, a 12-month regimen of isoniazid administered daily is recommended by the American Academy of Pediatrics (Peter, 1997).

Follow-up of HIV-Infected Persons Who Have Completed Preventive Therapy

Recommendation - A.II
Follow-up care, including chest x-rays and medical evaluations, is not necessary for patients who complete a course of TB preventive treatment, unless they develop symptoms of active TB disease or are subsequently reexposed to a person with infectious TB disease.

Follow-up of HIV-Infected Persons Who Are Candidates for, but Who Do Not Receive, TB Preventive Therapy

Recommendation - A.III
These persons should be assessed periodically (in intervals of less than 6 months) for symptoms of active TB as part of their ongoing HIV infection management. Clinicians should educate these persons about the symptoms of TB disease (e.g., cough with or without fever, night sweats, and weight loss) and advise them to seek immediate medical attention if they develop such symptoms. If persons

present with these symptoms, clinicians should always include TB disease in the differential diagnosis.

Definitions:

Strength of the Recommendation

A. Strong; should always be offered
B. Moderate; should usually be offered
C. Optional
D. Should generally not be offered
E. Should never be offered

Quality of Evidence Supporting the Recommendation

I. At least one randomized trial with clinical endpoints
II. Clinical trials with laboratory endpoints only or conducted only in populations not infected with human immunodeficiency virus
III. Expert opinion

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- The implementation of the recommendations will help prevent cases of drug-resistant tuberculosis (TB), reduce TB treatment failures, and diminish the adverse effects that TB has on HIV replication. Moreover, these guidelines will contribute to efforts to control TB and eliminate it from the United States by minimizing the likelihood of M. tuberculosis transmission, which will prevent the occurrence of new cases of TB.
- The effects of TB preventive therapy on mortality and progression of HIV infection appear to be limited, with the exception that such therapy can protect against the development of TB disease and its associated consequences. Moreover, the duration of this protective effect has not been clearly established for HIV-infected persons. Despite these limitations and

uncertainties, preventive therapy is recommended because its benefits in preventing TB disease are thought to be greater than the risks of serious treatment-related adverse events, and such therapy benefits society by helping to prevent the spread of infection to other persons in the community.

POTENTIAL HARMS

Antituberculosis Pharmacotherapy Side Effects

- Isoniazid. Rash, hepatic enzyme elevation, hepatitis, peripheral neuropathy, mild central nervous system effects, and drug interactions resulting in increased phenytoin (Dilantin) or disulfiram (Antabuse) levels
- Rifampin. Rash, hepatitis, fever, thrombocytopenia, flu-like symptoms associated with intermittent dosing, and orange-colored body fluids (secretions, urine, tears)
- Rifabutin. Rash, hepatitis, fever, thrombocytopenia, and orange-colored body fluids (secretions, urine, tears). With increased levels of rifabutin: severe arthralgias, uveitis, and leukopenia

*See special notice below

- Pyrazinamide. Gastrointestinal upset, hepatitis, rash, arthralgias, hyperuricemia, and gout (rare)
- Ethambutol. Optic neuritis (decreased red-green color discrimination), decreased visual acuity, and rash
- Streptomycin. Ototoxicity (hearing loss or vestibular dysfunction), and nephrotoxicity

*Special notice: 2004 Update

Rifamycins. Rifamycin resistance has developed during the treatment of TB in HIV-infected persons and has been associated with all rifamycins, particularly with highly-intermittent administration (once- or twice-weekly). In addition, rifamycin resistance has developed in patients who have advanced HIV disease and are receiving rifampin or rifabutin twice weekly. The ritonavir dose typically used for pharmacoenhancement of coadministered protease inhibitors (i.e., 100 mg or 200 mg twice daily), though less likely to produce adverse events than higher doses, still results in net CYP3A4 induction when used with rifampin.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The recommendations are not intended to substitute for the judgment of an expert physician. Management of HIV-related tuberculosis (TB) disease is complex, and clinical and public health consequences associated with treatment failure are serious. When possible, treatment of TB among HIV-infected persons should be directed by, or conducted in consultation with, a physician with extensive experience in the care of patients with these two diseases.

- The available data do not permit Centers for Disease Control and Prevention (CDC) to make a definitive recommendation regarding the issue of treatment length in patients with advanced HIV-related immunosuppression. However, the experts recommended that clinicians treating TB in patients with HIV infection should consider the factors that increase a person's risk for a poor clinical outcome (e.g., lack of adherence to TB therapy, delayed conversion of M. tuberculosis sputum cultures from positive to negative, and delayed clinical response) when deciding the total duration of TB therapy.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

RELATED QUALITY TOOLS

- AIDSinfo's Drug Database for Palm PDAs

- AIDSInfo Drug Database

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Centers for Disease Control and Prevention (CDC). Updated guidelines for the use of rifamycins for the treatment of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitors. Atlanta (GA):

Centers for Disease Control and Prevention (CDC); 2004 Jan 20. 6 p. [30 references]

Centers for Disease Control and Prevention. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: Principles of therapy and revised recommendations. MMWR Recomm Rep 1998 Oct 30;47(RR-20):1-58. [162 references] PubMed

Updated guidelines for the use of rifabutin or rifampin for the treatment and prevention of tuberculosis among HIV-infected patients taking protease inhibitors or nonnucleoside reverse transcriptase inhibitor. MMWR Morb Mortal Wkly Rep 2000 Mar 10;49(9):185-9. [10 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

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GUIDELINE COMMITTEE

Not stated

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

These guidelines update previous Centers for Disease Control and Prevention (CDC) recommendations for treating and preventing active tuberculosis (TB) among adults and children coinfected with human immunodeficiency virus (HIV):

- CDC. Tuberculosis and human immunodeficiency virus infection: Recommendations of the Advisory Committee for the Elimination of Tuberculosis (ACET). MMWR Morbid Mortal Wkly Rep 1989;38:236-8, 243-50.
- American Thoracic Society/CDC. Treatment of tuberculosis and tuberculosis infection in adults and children. Am J Respir Crit Care Med 1994;149:1359-74.
- CDC. Clinical update: impact of HIV protease inhibitors on the treatment of HIV-infected tuberculosis patients with rifampin. MMWR Morbid Mortal Wkly Rep 1996;45:921-5.

GUIDELINE AVAILABILITY

Electronic copies:

- The original guideline is available from the Centers for Disease Control and Prevention (CDC) Web site.
- The March 2000 "Notice to Readers: Updated Guidelines for the Use of Rifabutin or Rifampin for the Treatment and Prevention of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors." MMWR Morb Mortal Wkly Rep 2000 Mar 10;49(09);185-9 is available from the CDC Web site.
- The January 2004 "Notice to Readers: Updated Guidelines for the Use of Rifamycins for the Treatment of Tuberculosis Among HIV-Infected Patients Taking Protease Inhibitors or Nonnucleoside Reverse Transcriptase Inhibitors" MMWR Morb Mortal Wkly Rep 2004 Jan 23;53(02);37 is available from the CDC Web site.

Print copies: Available from the Centers for Disease Control and Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Essential components of a tuberculosis prevention and control program. MMWR Morb Mortal Wkly Rep 1995 Sep 8;44(RR-11):1-16. Available from the Centers for Disease Control and Prevention (CDC) Web site.
- Tuberculosis elimination revisited: Obstacles, opportunities, and a renewed commitment. MMWR Morb Mortal Wkly Rep 1999 Aug 13;48(RR-9):1-13. Available from the Centers for Disease Control and Prevention (CDC) Web site.

Print copies: Available from the Centers for Disease and Control Prevention, MMWR, Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

The following is also available:

- Prevention and treatment of tuberculosis among patients with infected human immunodeficiency virus: Principles of therapy and revised recommendations tool for Palm OS* or Pocket PC. The download is available from the AIDSinfo Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on March 20, 2000. The information was updated on September 21, 2000 and April 2, 2004. This summary was updated on January 21, 2005, following the release of a public health advisory from the U.S. Food and Drug Administration regarding the use of nevirapine. This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on Sustiva (efavirenz).

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